

RESEARCH MONOGRAPH . COMPOUND PROFILE

Beta-Hydroxybutyrate (BHB)

Beta-hydroxybutyric acid; the principal endogenous ketone body; a metabolic fuel and HDAC inhibitor with cognitive and longevity research interest.

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AUTHOR	Kodiac bioLabs Research
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ABSTRACT

Beta-hydroxybutyrate (BHB, (R)-3-hydroxybutyric acid; CAS 625-72-9; molecular formula $C_4H_8O_3$; molecular weight 104.10) is the principal endogenous ketone body, produced by hepatic mitochondrial beta-oxidation of fatty acids during fasting, ketogenic dieting, prolonged exercise, or insulin deficiency. The compound serves multiple roles: as a metabolic fuel substrate for brain, heart, and skeletal muscle (oxidized via beta-hydroxybutyrate dehydrogenase to acetoacetate, then to acetyl-CoA for TCA cycle entry); as an endogenous HDAC inhibitor (specifically class I HDACs at low millimolar concentrations); and as a ligand at hydroxycarboxylic acid receptor 2 (HCA2/GPR109A). Approved clinical use is the historical ketogenic diet for refractory pediatric epilepsy. Research interest spans neurodegenerative disease (Alzheimer, Parkinson), cognition, longevity (mTOR/autophagy modulation), and exercise performance (ketone supplementation in endurance sport). BHB salts (Ca, Na, Mg, K salts) and esters (1,3-butanediol esters of BHB) are sold as ergogenic supplements; the ketone monoester (HVMN Ketone, Delta G) is the most thoroughly studied. Plasma half-life of exogenous BHB is approximately 1 to 3 hours depending on formulation. Used as the canonical ketone body in metabolic and longevity research.

1. Compound Identification

Beta-Hydroxybutyrate (BHB) is described as endogenous ketone body / signaling metabolite. Beta-hydroxybutyric acid; the principal endogenous ketone body; a metabolic fuel and HDAC inhibitor with cognitive and longevity research interest.

1.1 Class summary

Endogenous ketone body / signaling metabolite

1.2 Subtitle

Beta-hydroxybutyric acid; the principal endogenous ketone body; a metabolic fuel and HDAC inhibitor with cognitive and longevity research interest.

2. Abstract

Beta-hydroxybutyrate (BHB, (R)-3-hydroxybutyric acid; CAS 625-72-9; molecular formula $C_4H_8O_3$; molecular weight 104.10) is the principal endogenous ketone body, produced by hepatic mitochondrial beta-oxidation of fatty acids during fasting, ketogenic dieting, prolonged exercise, or insulin deficiency. The compound serves multiple roles: as a metabolic fuel substrate for brain, heart, and skeletal muscle (oxidized via beta-hydroxybutyrate dehydrogenase to acetoacetate, then to acetyl-CoA for TCA cycle entry); as an endogenous HDAC inhibitor (specifically class I HDACs at low millimolar concentrations); and as a ligand at hydroxycarboxylic acid receptor 2 (HCA2/GPR109A). Approved clinical use is the historical ketogenic diet for refractory pediatric epilepsy. Research interest spans neurodegenerative disease (Alzheimer, Parkinson), cognition, longevity (mTOR/autophagy modulation), and exercise performance (ketone supplementation in endurance sport). BHB salts (Ca, Na, Mg, K salts) and esters (1,3-butanediol esters of BHB) are sold as ergogenic supplements; the ketone monoester (HVMN Ketone, Delta G) is the most thoroughly studied. Plasma half-life of exogenous BHB is approximately 1 to 3 hours depending on formulation. Used as the canonical ketone body in metabolic and longevity research.

3. Mechanism of Action

Endogenous ketone body; metabolic fuel substrate plus HDAC inhibition (class I) plus HCA2 receptor agonism. Multifactorial signaling beyond bioenergetic role.

The mechanistic profile described above represents the consensus position from peer-reviewed literature where available; for compounds with sparse formal characterization, this section reflects vendor-grade reports and structurally-related class pharmacology and should be interpreted with appropriate caution.

4. Pharmacokinetics and Routes of Administration

Pharmacokinetic data are summarized within the abstract for compounds with formal Phase 1 records. Compounds without published human pharmacokinetic studies are noted as such; investigators should treat the absence of data as a research limitation.

5. Reported Research Dose Ranges

Supplement (ketone esters/salts) 5 to 30 g per oral administration; ketogenic diet endogenous BHB 0.5 to 5 mM plasma.

Doses are scaled from clinical use where the compound is approved as a medicine, from Phase 2/3 trials where development advanced, or from rodent dose-response data scaled by allometric assumptions where the compound has no human clinical record. Investigators should treat dose ranges from research-chemical-grade vendors as starting points for their own pharmacokinetic and tolerability characterization rather than validated dosing recommendations.

6. Sourcing and Quality Verification

Investigators should obtain analytical confirmation of identity (mass spectrometry; for peptides, additionally amino acid analysis or N-terminal sequencing) and purity (HPLC area-percent, ideally greater than 95 percent) on every lot. Vendor certificates of analysis vary in quality; third-party analytical confirmation through independent laboratories (e.g., Janoshik Analytical, Anabolic Lab) is the gold standard for research-grade peptides and small molecules.

For compounds with established pharmaceutical-grade marketing in any jurisdiction, sourcing from the marketed product (where legal and accessible) provides the highest quality assurance.

7. Reconstitution and Handling

Peptides should be reconstituted in bacteriostatic water or sterile water for injection in the volume appropriate to the desired concentration; lyophilized peptides should be allowed to come to room temperature before reconstitution to minimize precipitation. Reconstituted peptides should be stored refrigerated and used within the timeframe specified by the manufacturer (typically 14 to 30 days for bacteriostatic water reconstitutions, shorter for sterile water).

Small molecules: storage conditions vary by compound; consult the certificate of analysis for the specific product. Most are stable at room temperature in dry, dark conditions; oxidation-sensitive compounds (e.g., catecholamine precursors) require cool storage and protection from light.

8. Stack Interaction Considerations

Investigators combining this compound with other research substances should consider receptor-level interactions (additive effects at shared targets), enzyme-level interactions (CYP-mediated drug-drug interactions where applicable), and pharmacodynamic interactions (additive sedation, additive serotonergic activity, additive hemodynamic effects).

The stack interaction section in published monographs of well-characterized compounds is necessarily incomplete for any specific combination; investigators should treat novel combinations with elevated caution and titrate gradually.

9. References

1. Newman JC, Verdin E. beta-Hydroxybutyrate: a signaling metabolite. *Annu Rev Nutr* 2017.
2. Cox PJ, et al. Nutritional ketosis alters fuel preference and thereby endurance performance in athletes. *Cell Metab* 2016.
3. Veech RL. The therapeutic implications of ketone bodies. *Prostaglandins Leukot Essent Fatty Acids* 2004.

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